Claims

1. A pharmaceutical composition for modulating at least one inflammatory response associated with human heparin binding protein (hHBP), said composition comprising an antibody against hHBP (SEQ ID NO: 1) or a fragment of said antibody, or an antibody against a homologue of hHBP or a fragment of said antibody, wherein the antibody (i) is capable of binding to an epitope within the sequence consisting of amino acid residues 1 to 19 or 45 to 226 according to SEQ ID NO: 1 and thereby stimulating at least one inflammatory response associated with hHBP, or (ii) is capable of binding to an epitope within the sequence consisting of amino acid residues 20 to 44 according to SEQ ID NO: 1 and thereby inhibiting at least one inflammatory response associated with hHBP.

2. The pharmaceutical composition according to claim 1, wherein the composition is for the stimulating at least one inflammatory response associated with human heparin binding protein (hHBP), said composition comprising an antibody against hHBP (SEQ ID NO: 1) or a fragment of said antibody, or an antibody against a homologue of hHBP or a fragment of said antibody, said antibody being capable of binding to an epitope within the sequence consisting of amino acid residues 1 to 19 or 45 to 226 according to SEQ ID NO: 1 and thereby stimulating at least one inflammatory response associated with hHBP.

3. The pharmaceutical composition according to claim 1, wherein the composition is for the inhibiting at least one inflammatory response associated with human heparin binding protein (hHBP), said composition comprising an antibody against hHBP (SEQ ID NO: 1) or a fragment of said antibody, or an antibody against a homologue of hHBP or a fragment of said antibody, said antibody being capable of binding to an epitope within the sequence comprising amino acid residues 20 to 44 according to SEQ ID NO: 1 and thereby inhibiting at least one inflammatory response associated with hHBP.

4. The pharmaceutical composition according to claim 1, 2 or 3, wherein the antibody is a monoclonal antibody.

5. The pharmaceutical composition according to claim 1 or 2, wherein the antibody is produced by a cell of clone F19A5B1 (ECACC Ass. No.: 03090301)

6. The pharmaceutical composition according to claim 1 or 3, wherein the antibody is produced by a cell of clone F19A5B4 (ECACC Ass. No.: 03090302)

7. The pharmaceutical composition according to claim 1, 2 or 3, wherein the antibody is a polyclonal antibody.

8. The pharmaceutical composition according to claim 1, 2 or 3, wherein the HBP homologue is porcine heparin binding protein (pHBP) (SEQ ID NO: 588).

9. The pharmaceutical composition according to claim 1, 2 or 3 wherein the HBP homologue is human neutrophil elastase (hNEL) (SEQ ID NO: 589).

10. The pharmaceutical composition according to claim 1, 2 or 3, wherein the modulating of at least one inflammatory response being

i) up- or down regulating the gene expression in the immune cells, preferably monocytes/macrophages, leading to secretion of endogenous inflammatory mediators including receptors for inflammatory mediators and transcription factors involved in the signal tranduction of the inflammatory mediators, activation of the production of bradykinin by the phase contact system, and/or

ii) increasing or decreasing the blood concentration of monocytes and/or local accumulation thereof at the sites of inflammation, and/or

iii) increasing or decreasing the life-time of monocytes, neutrophils and other immune cells due to inhibition of apoptosis, and/or

iv) activating or inhibiting the expression of adhesion molecules by the vascular endothelial cells, and/or

v) activating or inhibiting the contact phase system producing bradykinin leading to an increased vascular permeability, and/or

vi) increasing the phagocytic potential of monocytes/macrophages, and/or

vii) up-regulation of class-II MHC.

11. The pharmaceutical composition according to claim 10, wherein the immune cells are monocytes/macrophages.

12. The pharmaceutical composition according to claim 10, wherein the mediators are selected from the group comprising cytokines, selected from the group TNFalpha IL-1, IL-6, G-CSF, GM-CSF, M-CSF, chemokines selected from the group comprising IL-8, MCP-1, and receptors selected from the group comprising Tissue factor and IL-2Ralpha.

13. The pharmaceutical composition according to claim 10, wherein the adhesion molecules are selected from the group comprising PECAM, ICAM-1, E-selectins and VCAM-1.

14. The pharmaceutical composition according to any of the preceding claims 1, 2, 4, 5, 7, 8 or 9, wherein the antibody is a pro-inflammatory antibody capable of stimulating the at least one inflammatory response as defined in claims 10 -13 in the absence of bacterial products in the blood.

15. The pharmaceutical composition according to any of the preceding claims 1, 2, 4, 5, 7, 8 or 9, wherein the antibody is a pro-inflammatory antibody capable of stimulating the at least one inflammatory response as defined in claims 10 –13 in synergistic action with bacterial products present in the blood.

16. The pharmaceutical composition according to any of the claims 10 to 14, wherein the antibody is capable of stimulating the synthesis and/or release of cytokine IL-6.

17. The pharmaceutical composition according to claim 17, wherein the pro-inflammatory antibody is an antibody according to claim 5.

18 The pharmaceutical composition according to any of the preceding claims 1, 3, 4, 6, 7, 8 or 9, wherein the antibody is an anti-inflammatory antibody capable of inhibiting the at least one inflammatory response as defined in claims 10 -13 in the absence of bacterial products in the blood.

19 The pharmaceutical composition according to any of the preceding claims 1, 3, 4, 6, 7, 8 or 9, wherein the antibody is an anti-inflammatory antibody capable of inhibiting the at least one inflammatory response as defined in claims 10 -13 in the presence of bacterial products in the blood.

20 The pharmaceutical composition according to claims 18-19, wherein the antibody is an antibody according to claim 6.

21 The pharmaceutical composition according to claims 14-20, wherein the bacterial products are selected from the group consisting of LPS (Lipopolysaccharide), PGN (peptidoglycan), LTA (Lipotechoic acid), MDP (muramyldipeptide) and PCW (purified cell wall from bacteria).

22 The pharmaceutical according to claims 1, 2 or 3, wherein the antibody fragment being capable of binding to

(i) an epitope within the sequence consisting of amino acid residues 1 to 19 or 45 to 226 according to SEQ ID NO: 1 and thereby activating at least one inflammatory response according to claims 10-13, or

(ii) an epitope within the sequence consisting of amino acid residues 20-44 according to SEQ ID NO: 1 and thereby inhibiting at least one inflammatory response according to claims 10-13.

21. A pro-inflammatory monoclonal antibody produced by clone F19A5B1 (ECACC Ass. No.: 03090301).

22. An anti-inflammatory monoclonal antibody produced by clone F19A5B4 (ECACC Ass. No.: 03090302).

23. A cell producing the antibody according to claim 21.

24. A cell producing the antibody according to claim 22.

25. An antibody or fragment thereof, said antibody or said fragment is capable of binding to an epitope in hHBP, wherein said epitope being an epitope as according to claim 1, 2 or 3.

26. A recombinant protein comprising a fragment of the antibody of claim 21, said fragment being capable of binding to an epitope within the sequence consisting of amino acid residues 1 to 19 or 45 to 226 according to SEQ ID NO: 1 and thereby activating at least one inflammatory response as defined in claims 10-13.

27. A recombinant protein comprising a fragment of the antibody of claim 21, said fragment being capable of binding to an epitope within the sequence consisting of amino acid residues 20 to 44 according to SEQ ID NO: 1 and thereby inhibiting at least one inflammatory response as defined in claims 10-13.

28. A method for producing the antibody as defined in any of the preceding claims.

29. Use of a pharmaceutical composition according to claims 1, 2, 4, 5, 7, 8, 9, 14, 15, 16 or 17 for the stimulation of inflammatory response.

30. Use of a pharmaceutical composition according to claim 1,3, 4, 6, 7, 8, 9, 18, 19 or 20 for the inhibition of inflammatory response.

31. Use of antibody F19A5B1, a fragment thereof, a recombinant protein thereof, a recombinant protein of claim 26, or an antibody of claim 25 for the stimulation of inflammatory response.

32. Use of antibody F19A5B4, a fragment thereof, a recombinant protein thereof, a recombinant protein of claim 26, or an antibody of claim 25 for the inhibition of inflammatory response.

33. The use according to claims 29-32, wherein the inflammatory response is a response to bacterial infection.

34. The use according to claim 33, wherein the infection is a Gram negative bacterial infection.

35. The use according to claim 33, wherein the infection is a Gram positive bacterial infection

36. The use according to claims 29-33, wherein the inflammatory response is associated with sepsis, severe sepsis, septic shock and/or disseminated intravascular coagulation.

37. The use according to claims 29-33, wherein the inflammatory response is associated with meningitis.

38. The use according to claim 37, wherein meningitis is meningococcal meningitis.

39. The use according to claim 35, wherein the infection is by Pneumococcus pneumonae.

40. Use of antibody F19A5B1 for the manufacture of a medicament for treatment of individuals having suppressed immune system, cancer, autoimmune diseases and/or trauma.

41. Use of antibody F19A5B4 for the manufacture of a medicament for treatment of individuals to suppress a sustained inflammatory response.